

Refine Search

Search Results -

Terms	Documents
sh2 adj containing adj inositol adj phosphatase\$	5

Database:

US Pre-Grant Publication Full-Text Database
 US Patents Full-Text Database
 US OCR Full-Text Database
 EPO Abstracts Database
 JPO Abstracts Database
 Derwent World Patents Index
 IBM Technical Disclosure Bulletins

Search:

L1

Refine Search

Recall Text



Clear

Interrupt

Search History

DATE: Wednesday, February 04, 2004 [Printable Copy](#) [Create Case](#)

Set Name Query

side by side

Hit Count Set Name

result set

DB=USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=NO; OP=OR

L1 sh2 adj containing adj inositol adj phosphatase\$ 5 L1

END OF SEARCH HISTORY

Refine Search

Search Results -

Terms	Documents
ship same inhibit\$ and (allograft or rejection)	12

Database:

US Pre-Grant Publication Full-Text Database
 US Patents Full-Text Database
 US OCR Full-Text Database
 EPO Abstracts Database
 JPO Abstracts Database
 Derwent World Patents Index
 IBM Technical Disclosure Bulletins

Search:

L2

Refine Search

Recall Text

Clear

Interrupt

Search History

DATE: Wednesday, February 04, 2004 [Printable Copy](#) [Create Case](#)

Set Name Query
 side by side

Hit Count Set Name
 result set

DB=USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=NO; OP=OR

<u>L2</u>	ship same inhibit\$ and (allograft or rejection)	12	<u>L2</u>
<u>L1</u>	ship same inhibit\$ same (allograft or rejection)	1	<u>L1</u>

END OF SEARCH HISTORY

?s ship (s) (inhibit?) and (allograft or reject?)

Processing

Processed 10 of 37 files ...

Completed processing all files

118692 SHIP

7117567 INHIBIT?

1187 SHIP(S)INHIBIT?

148341 ALLOGRAFT

442663 REJECT?

S1 13 SHIP (S) (INHIBIT?) AND (ALLOGRAFT OR REJECT?)

?rd

...completed examining records

S2 4 RD (unique items)

?show files;ds;t/3,k/all

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File 266:FEDRIP 2004/Dec

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File 399:CA SEARCH(R) 1967-2004/UD=14006

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File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec

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 (c) 2004 BLHCIS
 File 444:New England Journal of Med. 1985-2004/Feb W2
 (c) 2004 Mass. Med. Soc.
 File 467:ExtraMED(tm) 2000/Dec
 (c) 2001 Informania Ltd.

Set	Items	Description
S1	13	SHIP (S) (INHIBIT?) AND (ALLOGRAFT OR REJECT?)
S2	4	RD (unique items)

>>>KWIC option is not available in file(s): 399

Set Items Description

--- -----
 ?s ship (s) (inhibit?) and (allograft or reject?)

Processing

Processed 10 of 37 files ...

Completed processing all files

118692 SHIP

7117567 INHIBIT?

1187 SHIP(S)INHIBIT?

148341 ALLOGRAFT

442663 REJECT?

S1 13 SHIP (S) (INHIBIT?) AND (ALLOGRAFT OR REJECT?)

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?show files;ds;t/3,k/all

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 File 91:MANTIS(TM) 1880-2003/Feb
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 File 444:New England Journal of Med. 1985-2004/Feb W2
 (c) 2004 Mass. Med. Soc.
 File 467:ExtraMED(tm) 2000/Dec
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Set	Items	Description
S1	13	SHIP (S) (INHIBIT?) AND (ALLOGRAFT OR REJECT?)
S2	4	RD (unique items)

>>>KWIC option is not available in file(s): 399

2/3,K/1 (Item 1 from file: 5)
 DIALOG(R)File 5:Biosis Previews(R)
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0013639526 BIOSIS NO.: 200200233037

Influence of SHIP on the NK repertoire and allogeneic bone marrow transplantation

AUTHOR: Wang Jia-Wang; Howson Julie M; Ghansah Tomar; Desponts Caroline; Ninos John M; May Sarah L; Nguyen Kim H T; Toyama-Sorimachi Noriko; Kerr William G (Reprint)

AUTHOR ADDRESS: Immunology Program, Departments of Interdisciplinary Oncology and Biochemistry, H. Lee Moffitt Comprehensive Cancer Center and Research Institute, University of South Florida, Tampa, FL, 33612, USA**
 USA

JOURNAL: Science (Washington D C) 295 (5562): p2094-2097 15 March, 2002
 2002

MEDIUM: print

ISSN: 0036-8075

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

...ABSTRACT: major histocompatibility complex (MHC) class I influence engraftment and graft-versus-tumor effects after allogeneic bone marrow transplantation. We find that SH2-containing inositol phosphatase (*SHIP*) influences the repertoire of NK receptors. In adult *SHIP*-/- mice, the NK compartment is dominated by cells that express two *inhibitory* receptors capable of binding either self or allogeneic MHC ligands. This promiscuous repertoire has significant functional consequences, because *SHIP*-/- mice fail to *reject* fully mismatched allogeneic marrow grafts and show enhanced survival after such transplants. Thus, *SHIP* plays an important role in two processes that limit the success of allogeneic marrow transplantation: graft *rejection* and graft-versus-host disease.

DESCRIPTORS:

DISEASES: graft *rejection*--

MESH TERMS: Graft *Rejection* (MeSH...

2/3,K/2 (Item 1 from file: 266)

DIALOG(R) File 266:FEDRIP

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00356977

IDENTIFYING NO.: 5R01HL72523-02 AGENCY CODE: CRISP

Role of SHIP in Control of NK Cell Function

PRINCIPAL INVESTIGATOR: KERR, WILLIAM G

ADDRESS: KERRW@MOFFITT.USF.EDU UNIVERSITY OF SOUTH FLORIDA 12902 MAGNOLIA
DR-IMMUN PROGRAM

PERFORMING ORG.: UNIVERSITY OF SOUTH FLORIDA, TAMPA, FLORIDA

SPONSORING ORG.: NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

DATES: 2007/01/02 TO 2006/30/06 FY : 2003

SUMMARY: DESCRIPTION (provided by the applicant): We find that the SH2-containing Inositol Phosphatase (*SHIP*) plays a crucial role in defining the *inhibitory* repertoire of NK cells in vivo. Four key findings made by our group support this hypothesis: (1) *SHIP* is recruited to both Ly49A and Ly49C in vivo, (2) the 85kD regulatory subunit of PI-3-Kinase (PI3K) is recruited to Ly49A in vivo, (3) Akt is constitutively active in *SHIP* -/- NK cells in vivo and (4) a subset of NK cells that co express Ly49A and Ly49C dominates the adult NK compartment in *SHIP* -/- mice. Ly49A and Ly49C can interact with self MHC ligands in our *SHIP* -/- mice, but also ligands of other MHC haplotypes. This promiscuous NK *inhibitory* repertoire has profound functional consequences as *SHIP* -/- mice fail to *reject* fully histo-incompatible marrow grafts. Strikingly, we find that survival of *SHIP* -/- mice is dramatically enhanced relative to wild-type littermates following transplantation of fully histo-incompatible marrow. These findings demonstrate a critical role for *SHIP* in two processes that limit the success of histo-incompatible marrow transplantation: graft *rejection* and graft-vs.-host disease. We now propose to confirm and extend our initial observations to gain a better understanding of how *SHIP* shapes the NK cell *inhibitory* repertoire and to better understand how this impacts marrow transplantation across major histocompatibility barriers. Specifically we will: (1) Determine the mechanism by which *SHIP* influences the NK *inhibitory* repertoire, (2) Determine whether a "self-restricted" NK *inhibitory* repertoire alters the ability of NK cells to respond to activating receptors and (3) Determine the mechanism for failure of graft *rejection* and abrogated GVHD during allogeneic BMT in SHIP -/- mice.

DESCRIPTORS: laboratory mouse; bone marrow transplantation; natural killer cell; leukocyte activation /transformation; phosphomonoesterase; inositol; graft versus host disease; transplantation immunology; enzyme activity; transplant *rejection*

2/3,K/3 (Item 1 from file: 357)

DIALOG(R) File 357:Derwent Biotech Res.

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0293601 DBR Accession No.: 2002-15448 PATENT

Suppressing or preventing *rejection* of transplant in patient, or treating or preventing graft-versus-host disease in patient comprises administration of a substance that inhibits SH2-containing inositol polyphosphatase function - vector mediated gene transfer and expression in host cell for transplantation therapy, drug screening and gene therapy

AUTHOR: KERR W G

PATENT ASSIGNEE: UNIV SOUTH FLORIDA 2002

PATENT NUMBER: WO 200224233 PATENT DATE: 20020328 WPI ACCESSION NO.:

2002-435045 (200246)

PRIORITY APPLIC. NO.: US 314099 APPLIC. DATE: 20010823

NATIONAL APPLIC. NO.: WO 2001US29158 APPLIC. DATE: 20010919

LANGUAGE: English

Suppressing or preventing *rejection* of transplant in patient, or treating or preventing graft-versus-host disease in patient comprises

administration of a substance that inhibits SH2-containing inositol polyphosphatase...

ABSTRACT: DERWENT ABSTRACT: NOVELTY - Suppressing or preventing *rejection* of transplant in a patient, or treating or preventing graft-versus-host disease (GVHD) in a patient having or in need of a transplant, by administering to the patient, a substance (I) that *inhibits* SH2-containing inositol polyphosphatase (*SHIP*) function. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a therapeutic composition comprising a substance that *inhibits* *SHIP* function in a carrier; (2) screening (M1) a substance suspected of *inhibiting* *SHIP* function involves providing a cell line that comprises an indicator of *SHIP* function; contacting the cell line with the substance; and measuring the response of the indicator to the substance, where the effectiveness of the substance as an *inhibitor* of *SHIP* function is assessed from the response to the indicator; (3) screening a candidate genetic construct for *inhibiting* *SHIP* function, involves providing an NK cell line that comprises an indicator of *SHIP* function, contacting the cell line with the genetic construct; and measuring the response of the indicator to the genetic construct; whereby the effectiveness of the genetic construct as an *inhibitor* of *SHIP* function is assessed from the response of the indicator; (4) screening (M2) a substance suspected of *inhibiting* *SHIP* function, involves allowing *SHIP* to react with a *SHIP* substrate in the presence of the substance, and taking a first measurement of signal that indicates the extent of the *SHIP*/substrate reaction; allowing *SHIP* to react with a *SHIP* substrate in the absence the substance; and taking a second measurement of the same signal that indicates the extent of the *SHIP*/substrate reaction; and comparing the first and second measurements, whereby a substance that *inhibits* *SHIP* function is selected; (5) a mouse cell (II) comprising a SHIPflox allele of a *SHIP* gene which includes a first exon and a promoter, where at least the first exon and the promoter have been deleted in the SHIPflox allele...

... mouse (V) derived from (IV). BIOTECHNOLOGY - Preferred Substance: (I) used in the method comprises a genetic construct that directs expression of an antagonist of a *SHIP* function. Preferably the genetic construct comprises an anti-sense polynucleotide, a polynucleotide that bind to *SHIP* mRNA, a nucleic acid that hybridizes to a *SHIP* mRNA, a recombinant retroviral vector, a ribozyme, an RNA aptamer, a peptidomimetic *inhibitor* of *SHIP* function, or their combination. Optionally (I) is the small molecule *inhibitor* of *SHIP* activity having a molecular weight of less than about 10000. Preferred Methods: In (M1), the substance is contacted with a natural killer (NK) cell line, and the response of the indicator (fluorogenic substrate of *SHIP*) to the substance is measured by flow cytometry or by a multi-well fluorescence detector. The indicator indicates Ly49 receptors, KIR, Fas, Fas ligand, or phosphatidyl serine in the extracellular leaflet of the plasma membrane. The substance which is contacted with the cell line is a small molecular *inhibitor* of *SHIP* activity, an anti-sense oligonucleotides, a peptidomimetic *inhibitor* of *SHIP* function, ribozymes, nucleic acid, polynucleotide, naked DNA, recombinant retroviral vector, RNA aptamer, anti-sense oligonucleotide, or their combination. Most preferably the small molecular *inhibitor* is a suicide substrate for *SHIP*. In (M2), *SHIP* is allowed to react with a *SHIP* substrate such as Shc, Grb2, the FcRIIB receptor, PIP3, and IP4, or their modification, in the presence of a substance such as small molecule *inhibitor* of *SHIP* activity, an oligonucleotide, a peptidomimetic *inhibitor* of *SHIP* activity, an oligonucleotide, a peptidomimetic *inhibitor* of *SHIP* function, a ribozymes, a polynucleotide, a polypeptide, an anti-*SHIP* antibody, or an RNA aptamer. Preferred Cell: (II) (preferably an embryonic stem cell) is homozygous with regard to the SHIPflox allele. Preferred Transgenic Mouse: (III) has a genotype of *SHIP*. (V) does not express *SHIP* protein. ACTIVITY - Immunosuppressive. No supporting data provided. MECHANISM OF ACTION - *SHIP* function *inhibitor*; suppressor of natural killer (NK) cell-mediator activities; antisense

therapy. A cohort of *SHIP*-/- mice and their *SHIP*+/- littermates were transplanted with whole bone marrow (BM) from BALB/C mice following lethal irradiation. Mice received 950 Rads prior to BM transplant. Fluorescence activated...

... vs. host re-population for B cells (B220+), myelo-granulocytic cells (Mac-1+/Gr-1+) or T cells (CD3+) in peripheral blood of a representative *SHIP*-/- BM transplantation survivor. 86% of the *SHIP* -/- mice survived lethal irradiation without developing GVHD out to 10 weeks post-transplant while only 36% survived in the *SHIP*+/- cohort. Analysis of the survival differences between the two cohorts using the Kaplan-Meier log-rank test confirmed that survival of *SHIP* -/- mice was dramatically enhanced relative to their *SHIP*+/- littermates (p=0.007). Nine of fourteen *SHIP*+/- mice died during the 10 week post-transplant period and prior to death exhibited one or more signs of severe GVHD up to 10 weeks post-transplant. USE - (I) is used in suppressing or preventing *rejection* of transplant e.g. bone marrow *allograft*, a solid organ *allograft* or xenotransplant, or an major histocompatibility complex (MHC) disparate marrow graft having MHC disparity of 1,2,3 or more allelic mismatches, in a patient having a disease such as cancer, autoimmune disease, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS). The method is also useful for suppressing or preventing *rejection* of a transplant in a patient who is in need of histo-incompatible organ transplant, where the method further involves the step of administering to...

2/3,K/4 (Item 1 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

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137346179 CA: 137(24)346179w PATENT

Control of NK cell function and survival by modulation of SHIP activity

INVENTOR(AUTHOR): Kerr, William G.; Ghansah, Tomar

LOCATION: USA

PATENT: U.S. Pat. Appl. Publ. ; US 20020165192 A1 DATE: 20021107

APPLICATION: US 97101 (20020314) *US PV233661 (20000919) *US PV314099

(20010823) *US 955174 (20010919)

PAGES: 28 pp., Cont.-in-part of U. S. Ser. No. 955,174. CODEN: USXXCO

LANGUAGE: English CLASS: 514044000; A61K-048/00A; A01K-067/027B

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